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United States Patent [19]

Bendig et al.

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Date of Patent:

Nov. 24, 1998

[54] HUMANIZED ANTIBODIES AGAINST LEUKOCYTE ADHESION MOLECULE

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[21] Appl. No.: 561,521

[51] Int C16

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Related U.S. Application Data 08

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	424/15	4.1: 424/173.1: 435/7.1: 435/7.2:

435/7.21; 435/7.24; 435/69.6; 435/172.3; 435/251.3; 435/320.1; 530/387.3; 530/388.73; 530/388.75; 530/388.22; 536/23.53

A61K 30/305: CO7K 16/28:

[58] Field of Search 424/130.1, 133.1, 424/141.1, 143.1, 144.1, 153.1, 154.1, 173.1; 435/69.6, 172.3, 252.3, 320.1, 7.1, 7.2, 7.21, 7.24; 536/23.4, 23.5, 23.53; 530/387.1, 387.3, 388.2, 388.22, 388.7, 388.73, 388.75

[56] References Cited

U.S. PATENT DOCUMENTS

5,260,210	11/1993	Rubin et al.	 435/240.23
5,530,101	6/1996	Queen et al.	 . 530/387.3

FOREIGN PATENT DOCUMENTS

239400	9/1987	European Pat. Off C12N 15/00
330506	•	European Pat. Off C07K 15/06
WO 90/07861	7/1990	WIPO C12P 21/00
WO 91/03252	2 3/1991	WIPO A61K 37/10
91/05038	3 4/1991	WIPO C12N 5/06
WO 93/15764	8/1993	WIPO A61K 39/395

OTHER PUBLICATIONS

Lisak et al. J. Neurol. Sciences 62: 281-293 (1983). Teitelbaum et al. PNAS 89: 137-141 (1992). Weiner et al. Science 259: 1321-1324 (1993) Racke et al. J. Neuroimmunol. 46: 175-184 (1993). Karussis et al PNAS 90: 6400-6404 (1993).

Cannella et al. Ann Neurol. 37: 424-435 (1995).

Washington et al. Ann Neurol 35: 89-97 (1994).

Dore-Duffy et al. in Frontiers in Cerebral Vascular Biology: Transport and its Regulation (eds) Dreues and Betz Plenum Press Ny 1993 pp. 243-248.

Monshizadegan et al., "VLA-4-dependent adhesion activities of U937 cells and guinea peg bronchoalveolar lavage leukocytes", 1993, Agents Actions 39, pp. C177-C179.

Kettleborough et al., "Humanization of a mouse monoclonal antibody by CDR-grafting the importance of framework residues on loop conformation", 1991, Protein Engineering, vol. 4, No. 7, pp. 773-783.

Yednock et al. "Prevention of experimental autoimmune encephalomyelitis by antibodies against α4β1 integrin", 1991, Letters to Nature, vol. 356, pp. 63-66.

W. J. Harris and S. Emery, "Therapeutic antibodies-the coming of age", 1993, Tibiech, vol. 11, pp. 42-45.

S. C. Emery and J. R. Adair, "Humanised monoclonal antibodies for therapeutic applications", 1994, Exp. Opin. Invest. Drugs, vol. 3, pp. 241-251.

S. M. Edgington, "How Sweet It Is: Selectin-Mediating Drugs", 1992, Bio/Technology, vol. 10, pp. 383-389.

Elices et al., "VCAM-1 on Activated Endothelium Interacts with the Leukocyte Integrin VLA-4 at a Site Distinct form the VLA-4/Fibronectin Binding Site", 1990, Cell, vol. 60, pp. 577-584.

Dijkstra et al., "Multiple sclerosis: some possible therapeutic opportunities", 1993, *Tips Reviews*, vol. 14, pp. 124-129.

A. Mountain and J.R. Adair, "Engineering Antibodies for Therapy", 1992, Biotech Genetic Engineering Reviews, vol. 10, pp. 10-13.

P.A. Ward and M.S. Mulligan, "Blocking of adhesion molecules in vivo as anti-inflammatory therapy", 1994, Therapeutic Immunol, vol. 10, pp. 165-171.

L. K. Jolliffe, "Humanized Antibodies: Enhancing Therapeutic Utility Through Antibody Engineering", 1993, Intern Rev Immunol, vol. 10, pp. 241-250.

Albelda Faseb J. 8: 504-512 (1994).

Kahan Curr Opin Immunology 4: 553-560 (1992).

Natanson et al. Ann Intern Med. 120: 771-783 (1994).

Dalakas Ann. Neurol. 37(51): 52-513 (1995).

Paul (ed) Fundamental Immunology Raven Press NY 1993 p. 242 only.

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ABSTRACT

The invention provides humanized immunoglobulins that specifically bind to the VLA-4 ligand, and methods of treatment using the same. The methods are particularly useful for treatment of multiple sclerosis.

29 Claims, 16 Drawing Sheets